CLAIMS

1. An apparatus for performing the polymerase chain reaction in a plurality of liquid reaction mixtures; said apparatus including a plurality of vials containing such liquid reaction mixtures, said vials having an upper portion and a lower portion; said apparatus comprising:

an assembly for cycling said vials through a series of temperature excursions;

a cover for applying a seating force directly to said vials and for applying a constant temperature to the upper portion of said vials; and

a computing apparatus for controlling said temperature excursions of said assembly and said constant temperature of said cover.

2. The apparatus of claim 1 wherein said assembly comprises:

a sample block for receiving said vials;

a plurality of thermal electric devices;

a heat sink;

a clamping mechanism positioned so as to clamp said Peltier thermal electric devices between said sample block and said heatsink;

a heater positioned loosely around the perimeter of said sample block; and

a pin having a first end and a second end, said first end in close contact with said sample block and said second end in close contact with said heatsink so as to provide a thermal path between said sample block and said heatsink.

3. The apparatus of claim 2 wherein said sample block comprises:

a plurality of sample wells, for receiving sample vials, each well having a top and bottom;

an upper support plate connecting the tops of said sample wells.

4. The apparatus of claim 3 wherein said upper support plate and said sample wells are electroformed as a single piece.

5. The apparatus of claim 3 wherein said sample block is comprised of silver.

C1 6. The apparatus of claim 3 wherein said sample wells are arranged in an 8 x 12 array.

7. The apparatus of claim 3 wherein sample block is rectangular.

Sub A3 8. The apparatus of claim 2 wherein said plurality of Peltier thermoelectric devices are matched to provide a temperature within 0.2 C for a given input current.

A ~~9.~~ The apparatus of claim ~~2~~ 1 wherein said Peltier thermoelectric devices comprise:

Sub C1

a first ceramic layer having bonded copper traces;

a second ceramic layer having bonded copper traces, said second ceramic layer comprising a plurality of ceramic elements; and

a plurality of bismuth telluride pellets positioned between said first ceramic layer and said second ceramic layer and soldered to said bonded copper traces on said first and second ceramic layers.

10. The apparatus of claim 9 wherein the ceramic of said first and second layer is alumina.

11. The apparatus of claim 9 wherein the ceramic layers have a thickness of 0.508mm.

12. The apparatus of claim 9 wherein said bismuth telluride pellets are soldered using high temperature solder.

Sub A4 13. The apparatus of claim 9 wherein the resistivity of the devices is determined from the equation:

$$R = nr(h/A)$$

where R is the resistivity of the device, n is the number of pellets, r is the resistivity of the bismuth telluride being used, h is the height of the pellet and A is the cross sectional area of the bismuth telluride.

A4 end

A ~~14.~~ The apparatus of claim ~~2~~ 1 wherein said heatsink comprises:

a plate having a top side and a bottom side;

a plurality of fins extending perpendicularly from said bottom side;

a trench extending around the perimeter of said top side to impede heat loss from said perimeter;

a fan placed in close proximity to said fins to control air flow through said fins; and

a recess within said plate for receiving a temperature sensor.

Sub C1

A 15. The assembly of claim ~~2~~ 1 wherein said clamping mechanism comprises:

a spine and said spine having a plurality of openings in said spine for receiving fasteners;

a plurality of fingers extending laterally from said spine.

16. The apparatus mechanism of claim 15 wherein said spine is rectangular in shape.

17. The apparatus mechanism of claim 15 wherein said fingers are rectangular in shape.

18. The apparatus of claim 15 wherein said fingers have a top and a bottom and are tapered so as to have less width at said top than at said bottom.

19. The apparatus of claim 15 wherein said fingers have a first end protruding laterally from said spine and a protrusion extending downward from said first end.

20. The apparatus of claim 15 wherein said fingers have a beveled front edge.

21. The apparatus of claim 15 wherein each of said openings are located in close proximity to a corresponding finger.

22. The apparatus of claim ~~2~~ 1 wherein said heater comprises an electrically resistive path embedded in a frame shaped film carrier.

23. The apparatus of claim 22 wherein said electrically resistive path comprises a first set of sections located on opposite sides of said frame shaped carrier having a first power density and a second set of sections located on opposite sides of said frame shaped having a second power density.

24. The apparatus of claim ~~2~~ 1 further comprising an associated memory device capable of storing data related to said assembly.

25. The apparatus of Claim 1 wherein said cover comprises:

a platen, vertically and horizontally displaceable in relationship to said vials, said platen including:

an array of openings corresponding to locations of said vials, said openings having a perimeter corresponding to a perimeter of said vials;

a skirt extending downward around the perimeter of said platen, said skirt having dimensions corresponding to the perimeter of a standard microtiter tray, said skirt constructed to engage said perimeter of said tray during vertical displacement of said platen, causing said openings in said platen to engage said perimeter of said vials, applying a seating force on said vials for maintaining a snug fit between walls of said sample vials and said assembly for receiving said sample vials;

means for forcibly lowering said platen to maintain said seating force; and

C1

heating means positioned in close contact with said platen to maintain said platen at a constant temperature.

Sub A5

26. The apparatus of claim 1 wherein said assembly comprises of at least one devise for changing the temperature of said apparatus further comprising a system for measuring the AC resistance of said thermal electric device.

Sub C1

27. The apparatus of claim 26 wherein at least one device has a first heating and cooling surface and a second heating and cooling surface, said system comprising:

a first temperature sensor positioned so as to be in thermal communication with said first heating and cooling surface;

a second temperature sensor positioned so as to be in thermal communication with said second heating and cooling surface;

A a bi-polar amplifier circuit for providing power to said thermoelectric ~~thermal electric~~ device;

A a circuit for sensing AC voltage across said thermoelectric ~~thermal electric~~ device and producing a DC voltage representing said AC voltage;

A a circuit for sensing AC current through said thermoelectric ~~thermal electric~~ device and producing a DC voltage representing said AC current;

a microcontroller programmed to receive said signals from said first and second temperature sensors;

said microcontroller further programmed to cause said bi-polar amplifier to

A provide power to said thermoelectric ~~thermal electric~~ device so that said first and second temperature sensor signals indicate equal temperatures;

said microcontroller further programmed to cause an AC voltage to be superimposed on said bi-polar amplifier power;

said microcontroller further programmed to receive said voltages produced by said circuit for sensing AC voltage and from said circuit for sensing AC current;

said microcontroller further programmed to calculate the AC resistance of said A ~~thermal electric~~ thermoelectric device from said voltages;

said microcontroller further programmed to compensate for ambient temperature C error by performing a polynomial calculation; and

said microcontroller further programmed to store said compensated AC resistance measurement.

Sub A6 28. A method for measuring the AC resistance of a thermal electric device having a first heating and cooling surface and a second heating and cooling surface, said method comprising:

measuring the temperature of said first heating and cooling surface;

measuring the temperature of said second heating and cooling surface;

applying power to said Peltier thermal electric device to cause said first heating and cooling surface and said second heating and cooling surface to attain the same temperature;

applying an AC voltage across said thermal electric device;

measuring said AC voltage across said thermal electric device;

measuring AC current through said thermal electric device;

calculating the AC resistance of said thermal electric device from said measured AC voltage and said measured AC current.

Sub C 29. The method of claim 28, further comprising:

performing a calculation for compensating for ambient temperature error to calculate a compensation AC resistance measurement; and

storing said compensated AC resistance measurement.

Sub A7 30. A method for achieving linear temperature transitions utilizing a thermal electric device having at least a first heating and cooling surface and a second heating and cooling surface and being operated in a manner causing said first surface to be higher in

temperature and said second surface to be lower in temperature relative to each other, said method comprising the following steps:

determining a desired heat flow from said lower temperature surface;

determining electrical resistance of said thermal electric device as a function of temperature;

determining the Seebeck coefficient of said thermal electric device as a function of temperature;

determining the conduction of said thermal electric device as a function of temperature;

measuring the temperature of said lower temperature surface;

measuring the temperature of said higher temperature surface;

A7

calculating the average temperature of said lower temperature surface and said higher temperature surface; and

calculating the current required to achieve said desired heat flow as a function of said electrical resistance of said thermal electric device as a function of temperature, said Seebeck coefficient of said thermal electric device as a function of temperature, said conductance of said thermal electric device as a function of temperature, said temperature of said lower temperature surface, said temperature of said higher temperature surface, and said average of said lower temperature surface and said higher temperature surface.

31. A method for determining the temperature of a mixture in a sample vial, said vial having an upper portion and a lower portion an contained in an apparatus comprising;

as assembly for cycling said vials through a series of temperature excursions, said assembly further comprising a sample block for receiving said vials;

a cover for applying a seating force on said vials and for applying a constant temperature to the upper portion of said vials; and

a computing apparatus for controlling said temperature excursions of said assembly and said constant temperature of said cover.

said method comprising:

measuring the temperature of said sample block;

measuring the temperature applied by said cover;

determining the thermal resistance of said vial between said sample block and said mixture;

determining the thermal resistance of air in parallel with said vial between said mixture and said cover;

A7 end

determining the thermal capacitance of said mixture;

determining the thermal capacitance of said vial between said mixture and said cover; and

calculating the temperature of said mixture as a function of said temperature of said sample block, said temperature applied by said cover, said thermal resistance of said vial between said sample block and said mixture, said thermal resistance of air in parallel with said vial between said mixture and said cover, said thermal capacitance of said mixture and said thermal capacitance of said vial between said mixture and said cover.

32. A method of calibrating an assembly for cycling samples through a series of temperature excursions comprising a sample block for receiving vials, a plurality of thermal electric devices, a heat sink, a clamping mechanism positioned so as to clamp said ~~Peltier~~ thermal electric devices between said sample block and said heatsink, and a memory device capable of storing data related to said assembly, said method comprising:

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applying power to said thermal electric devices, causing said assembly to cycle through a desired series of temperature excursions

measuring the actual temperature excursions

comparing said actual temperature excursions with said desired temperature excursions

adjusting said power applied to said thermal electric devices so that said actual temperature excursions match said desired temperature excursions

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recording said adjusted power in said memory device located on said assembly for further utilization in obtaining said desired series of temperature excursions

no period

Sub B1

33. An assembly for cycling vials of reaction mixtures through a series of temperature excursions comprising:

a sample block for receiving vials of reaction mixtures;

a plurality of thermal electric devices;

a heat sink;

a clamping mechanism positioned so as to clamp said thermal electric devices between said sample block and said heatsink;

a heater positioned around the perimeter of said sample block; and

a pin having a first end and a second end, said first end in close contact with said sample block and said second end in close contact with said heatsink so as to provide a thermal path between said sample block and said heatsink;

a computing apparatus for controlling said temperature excursions of said assembly and said heater.

34. A sample block for holding sample vials comprising:

a plurality of sample wells, for receiving sample vials, each well having a top and bottom;

an upper support plate connecting the tops of said sample wells; and

a bottom plate connecting the bottom of said sample wells

35. The sample block of claim 34 wherein said upper support plate and said sample wells are electroformed as a single piece.

36. The sample block of claim 34 wherein said sample block is comprised of silver.

37. The sample block of claim 34 wherein said sample wells are arranged in an 8 x 12 array.

38. The sample block of claim 34 wherein sample block is rectangular.

39. A heatsink assembly comprising:

a plate having a top side and a bottom side;

a plurality of fins extending perpendicularly from said bottom side;

a trench extending around the perimeter of said top side to impede heat loss from said perimeter;

a fan placed in close proximity to said fins to control air flow through said fins; and

a recess within said plate for receiving a temperature sensor.

A 40. An apparatus for measuring the AC resistance of a thermoelectric ~~Peltier thermal electric~~ device having a first heating and cooling surface and a second heating and cooling surface, said system comprising:

a first temperature sensor positioned so as to be in thermal communication with said first heating and cooling surface;

a second temperature sensor positioned so as to be in thermal communication with said second heating and cooling surface;

a bi-polar amplifier circuit for providing power to said thermal electric device;

A a circuit for sensing AC voltage across said thermoelectric ~~thermal electric~~ device and producing a DC voltage representing said AC voltage;

A a circuit for sensing AC current through said thermoelectric ~~thermal electric~~ device and producing a DC voltage representing said AC current;

a microcontroller programmed to receive said signals from said first and second temperature sensors;

said microcontroller further programmed to cause said bi-polar amplifier to
A provide power to said thermoelectric ~~thermal electric~~ device so that said first and second temperature sensor signals are equal;

said microcontroller further programmed to cause an AC voltage to be superimposed on said bi-polar amplifier power;

said microcontroller further programmed to receive said voltages produced by said circuit for sensing AC voltage and from said circuit for sensing AC current;

said microcontroller further programmed to calculate the AC resistance of said ~~thermal electric~~ thermoelectric device from said voltages;

said microcontroller further programmed to compensate for ambient temperature error by performing a polynomial calculation; and

said microcontroller further programmed to store said compensated AC resistance measurement.

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